#7

Figure 1

Streptococcus mutans
***ComCDE* Operon**

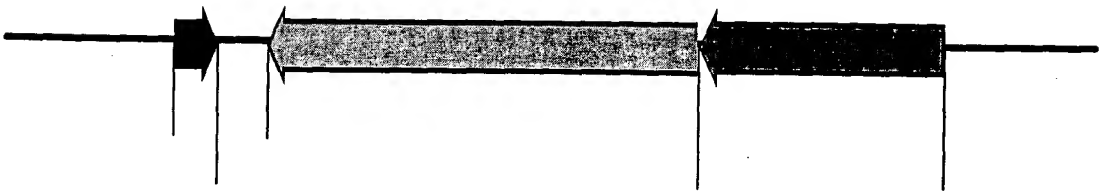

Figure 2

A.

[ATGAAAAAAACACTATCATTAAAAAATGACTTTAAAGAAATTAAGACTGATGAATTAG
AGATTATCATTGGCGGA (AGCGGAAGCCTATCAACATTTTTCCGGCTGTTTAACAGAAG
TTTTACACAAGCTTTGGGAAAA)] TAA

B.

AGCGGAAGCCTATCAACATTTTTCCGGCTGTTTAACAGAAGTTTTACACAAGCTTTGGG
AAAA

C.

[ATGAATGAAGCCTTAATGATACTTTCAAATGGTTTATTAACTTATCTAACCGTTCTAT
TTCTCTTGTTTCTATTTTCTAAGGTAAGTAATGTCACTTTATCGAAAAAGGAATTAACT
CTTTTTTCGATAAGCAATTTTCTGATAATGATTGCTGTTACGATGGTGAACGTAAACCT
GTTTTATCCTGCAGAGCCTCTTTATTTTATAGCTTTATCAATTTATCTTAATAGACAGA
ATAGTCTTTCTCTAAATATATTTTATGGTCTGCTGCCTGTTGCCAGTTCTGACTTGTTT
AGGCGGGCAATCATATTCTTTATCTTGGATGGAACTCAAGGAATTGTAATGGGCAGTAG
CATTATAACCACCTATATGATCGAGTTTGCAGGAATAGCGCTAAGTTACCTCTTTCTCA
GTGTGTTCAATGTTGATATTGGTCGACTTAAAGATAGTTTGACCAAGATGAAGGTCAAA
AAACGCTTGATTCCAATGAATATTACTATGCTTCTATACTACCTTTTAATACAGGTATT
GTATGTTATAGAGAGTTATAATGTGATACCGACTTTAAAATTTCGTAAATTTGTCGTTA
TTGTCTATCTTATTTTATTTTTGATTCTGATCTCATTTTTAAGCCAATATACCAAACAA
AAGGTTCAAAATGAGATAATGGCACAAAAGGAAGCTCAGATTCGAAATATCACCCAGTA
TAGTCAGCAAATAGAATCTCTTTACAAGGATATTCGAAGTTTCCGCCATGATTATCTGA
ATATTTTAACTAGCCTCAGATTAGGCATTGAAAATAAAGATTTAGCTAGTATTGAAAAG
ATTTACCATCAAATCTTAGAAAAAACAGGACATCAATTGCAGGATACCCGTTATAATAT
CGGCCATCTAGCTAATATTCAAAACGATGCTGTCAAGGGTATCTTGTCAGCAAAAATCT
TAGAAGCTCAGAATAAAAAGATTGCTGTCAATGTAGAAGTCTCAAGTAAAATACAACTG
CCTGAGATGGAGTTGCTTGATTTCATTACCATACTTTCTATCTTGTGTGATAATGCCAT
TGAGGCTGCTTTCGAATCATTAAATCCTGAAATTCAGTTAGCCTTTTTTAAGAAAAATG
GCAGTATAGTCTTTATCATTCAGAATTCCACCAAAGAAAAACAAATAGATGTGAGTAAA
ATTTTTAAAGAAAACTATTCCACTAAAGGCTCCAATCGCGGTATTGGTTTAGCAAAGGT
GAATCATATTCTTGAACATTATCCCAAAACCAGTTTACAAACAAGCAATCATCATCATT
TATTCAAGCAACTCCTAATAATAAAA] TAG

D.

[ATGATTTCTATTTTTGTATTGGAAGATGATTTTTTACAACAAGGACGTCTTGAAACCA
CCATTGCAGCTATCATGAAAGAAAAAAATTGGTCTTATAAAGAATTGACTATTTTTGGA
AAACCACAACAACTTATTGACGCTATCCCTGAAAAGGGCAATCACCAGATTTTCTTTTT
GGATATTGAAATCAAAAAAGAGGAAAAGAAAGGACTGGAAGTAGCCAATCAGATTAGAC
AGCATAATCCTAGTGCAGTTATTGTCTTTGTCACGACACATTCTGAGTTTATGCCCCTC
ACTTTTCAGTATCAGGTATCTGCTTTGGATTTTATTGATAAATCTTTGAATCCTGAGGA
GTTCTCCCACCGCATTGAATCAGCGCTGTATTATGCTATGGAAAACAGCCAGAAGAATG
GTCAATCAGAGGAACTTTTTATTTTCCATTCATCTGAAACTCAGTTTCAGGTCCCTTTT
GCTGAGATTCTGTATTTTGAAACATCTTCAACAGCCCATAAGCTCTGCCTTTATACTTA
TGATGAACGGATTGAATTCTACGGCAGTATGACTGACATTGTTAAAATGGATAAGAGAC

Figure 2 (cont'd)

TTTTTCAGTGCCATCGCTCTTTTATTGTCAATCCTGCCAATATTACCCGTATTGATCGG
AAAAAACGCTTGGCCTATTTTCGAAATAATAAGTCTTGTCTTATTTCACGAACTAAGTT
AACAAAACTGAGAGCTGTGATTGCTGATCAAAGGAGAGCAAAA] TGA

Figure 3

A.

MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK

B.

MNEALMILSNGLLTYLTVLFLLFLFSKVSNVTLSKKELTLFSISNFLIMIAVTMVNVNL
FYPAEPLYFIALSIYLNRQNSLSLNIFYGLLPVASSDLFRRAIIFFILDGTQGIVMGSS
IITTYMIEFAGIALSYLFLSVFNVDIGRLKDSLTKMKVKKRLIPMNITMLLYYLLIQVL
YVIESYNVIPTLKFRKFVVIVYLILFLILISFLSQYTKQKVQNEIMAQKEAQIRNITQY
SQQIESLYKDIRSFRHDYLNILTSLRLGIENKDLASIEKIYHQILEKTGHQLQDTRYNI
GHLANIQNDAVKGILSAKILEAQNKKIAVNVEVSSKIQLPEMELLDFITILSILCDNAI
EAAFESLNPEIQLAFFKKNGSIVFIIQNSTKEKQIDVSKIFKENYSTKGSNRGIGLAKV
NHILEHYPKTSLQTSNHHHLFKQLLIIK

C.

MISIFVLEDDFLQQGRLETTIAAIMKEKNWSYKELTIFGKPQQLIDAIPEKGNHQIFFL
DIEIKKEEKKGLEVANQIRQHNPSAVIVFVTTHSEFMPLTFQYQVSALDFIDKSLNPEE
FSHRIESALYYAMENSQKNGQSEELFIFHSSETQFQVPFAEILYFETSSTAHKLCLYTY
DERIEFYGSMTDIVKMDKRLFQCHRSFIVNPANITRIDRKKRLAYFRNNKSCLISRTKL
TKLRAVIADQRRAK

Figure 4

A.

```
BM71 CSP      1 MKKTPSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK 46
GB14 CSP      1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK 46
H7 CSP        1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK 46
JH1005 CSP    1 MKKTLSLKNDFKEIKTDELEIIIGGSGTLSTFFRLFNRSFTQA    43
LT11 CSP      1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK 46
NG8 CSP       1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK 46
UAB159 CSP    1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK 46
                **** **********************.***************
```

B.

```
consensus: 1 MKKTLSLKNDFKEIKTDELEIIIGG SGSLSTFFRLFNRSFTQALGK 46
predicted cleavage site:             ^
```

Figure 5

SGSLSTFFRLFNRSFTQALGK

Figure 6

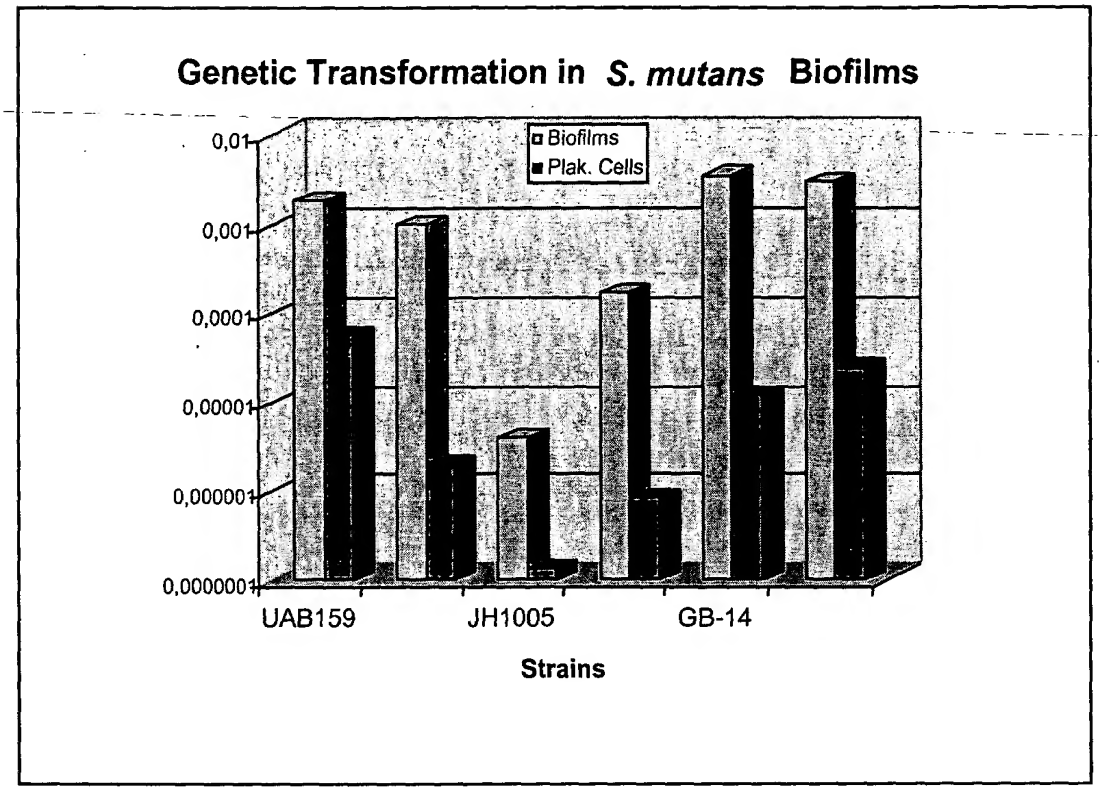
Genetic Transformation in S. mutans Biofilms
Biofilms
Plak. Cells
0,01
0,001
0,0001
0,00001
0,000001
0,0000001
UAB159
JH1005
GB-14
Strains

Figure 7

Strain	Peptide added Number of Transformants/Recipients	No peptide Number of Transformants/Recipients
UAB15	4.65×10^{-1}	1.78×10^{-6}
JH1005[2]	6.98×10^{-2}	0

[1]The final concentration of SCSP used was 500 ng/ml.
The strain contains a nonsense mutation in the *comC* gene encoding the CSP.

Figure 8

ComC region

ComC Primer Pair: F5-B5

[F5] 23406-23424 5'- AGTTTTTTGTCTGGCTGCG -3'
19 nt forward primer
pct G+C: 47.4 Tm: 50.5

[B5] 24056-24037 5'- TCCACTAAAGGCTCCAATCG -3'
20 nt backward primer
pct G+C: 50.0 Tm: 51.9

651 nt product for F5-B5 pair (23406-24056)
Optimal annealing temp: 50.3
pct G+C: 30.9 Tm: 71.5

ComD region

ComD Primer Pair: F1-B1

[F1] 392-415 5'- CGCTAAGTTACCTCTTTCTCAGTG -3'
24 nt forward primer
pct G+C: 45.8 Tm: 51.6

[B1] 683-663 5'- GCTTCCTTTTGTGCCATTATC -3'
21 nt backward primer
pct G+C: 42.9 Tm: 50.8

292 nt product for F1-B1 pair (392-683)
Optimal annealing temp: 49.5
pct G+C: 30.8 Tm: 70.2

ComE region

ComE Primer Pair: F1-B1

[F1] 145-165 5'- CCTGAAAAGGGCAATCACCAG -3'
21 nt forward primer
pct G+C: 52.4 Tm: 55.9

[B1] 606-585 5'- GCGATGGCACTGAAAAAGTCTC -3'
22 nt backward primer
pct G+C: 50.0 Tm: 55.4

462 nt product for F1-B1 pair (145-606)
Optimal annealing temp: 53.6
pct G+C: 38.3 Tm: 74.1

Figure 9

Sequence Range: 1 to 2557

```
          10         20         30         40         50
ACATTATGTGTCCTAAGGAAAATATTACTTTTTCAAGAAAATCCATGATT
TGTAATACACAGGATTCCTTTTATAATGAAAAAGTTCTTTTAGGTACTAA
                              <K  K  L  F  I  W  S  K
                           <_____________________________

          60         70         80         90         100
TTTTCATAAAAAATAGTATACTAATTATAATCAAAAAAAGGAGATATAAA
AAAAGTATTTTTTATCATATGATTAATATTAGTTTTTTTCCTCTATATTT
 <K  M  F  F  L  I  S  I  I  I  L  F  L  L  Y  L
<_____________________________________________________

          110        120        130        140        150
ATGAAAAAAACACTATCATTAAAAAATGACTTTAAAGAAATTAAGACTGA
TACTTTTTTTGTGATAGTAATTTTTTACTGAAATTTCTTTAATTCTGACT
 M  K  K  T  L  S  L  K  N  D  F  K  E  I  K  T  D>
_____________________ORF RF[2] _____________________>
<I  F  F  V  S  D  N  F  F  S  K  L  S  I  L  V  S
<_____________________________________________________

          160        170        180        190        200
TGAATTAGAGATTATCATTGGCGGAAGCGGAAGCCTATCAACATTTTTCC
ACTTAATCTCTAATAGTAACCGCCTTCGCCTTCGGATAGTTGTAAAAAGG
  E  L  E  I  I  I  G  G  S  G  S  L  S  T  F  F>
_____________________ORF RF[2] _____________________>
<S  N  S  I  I  M
<_____________________

          210        220        230        240        250
GGCTGTTTAACAGAAGTTTTACACAAGCTTTGGGAAAATAAGATAGGCTA
CCGACAAATTGTCTTCAAAATGTGTTCGAAACCCTTTTATTCTATCCGAT
R  L  F  N  R  S  F  T  Q  A  L  G  K>
_____________ORF RF[2] _____________>

          260        270        280        290        300
ACATTGGAATAAAACAAGGCTGGATTTATTATTCCAGCCTTTTTAAATGT
TGTAACCTTATTTTGTTCCGACCTAAATAATAAGGTCGGAAAAATTTACA

          310        320        330        340        350
AAAATAAAAATACAGGGTTAAATAATCAAGTGTGCTGTCGTGGATGAGAA
TTTTATTTTTATGTCCCAATTTATTAGTTCACACGACAGCACCTACTCTT

          360        370        380        390        400
GATAAAACTATCTCTTAGAGAATAGGCCTCCTCTATTTTATTATTAGGAG
CTATTTTGATAGAGAATCTCTTATCCGGAGGAGATAAAATAATAATCCTC
                                        <K  I  I  L  L
                                     <____ORF RF[____

          410        420        430        440        450
TTGCTTGAATAAATGATGATGATTGCTTGTTTGTAAACTGGTTTTGGGAT
AACGAACTTATTTACTACTACTAACGAACAAACATTTGACCAAAACCCTA
<Q  K  F  L  H  H  H  N  S  T  Q  L  S  T  K  P  Y
```

Figure 9 (cont'd - 1)

```
<_____ORF RF[4] C_____

       460        470        480        490        500
AATGTTCAAGAATATGATTCACCTTTGCTAAACCAATACCGCGATTGGAG
TTACAAGTTCTTATACTAAGTGGAAACGATTTGGTTATGGCGCTAACCTC
 <H  E  L  I  H  N  V  K  A  L  G  I  G  R  N  S
<_____ORF RF[4] C_____

       510        520        530        540        550
CCTTTAGTGGAATAGTTTTCTTTAAAAATTTTACTCACATCTATTTGTTT
GGAAATCACCTTATCAAAAGAAATTTTTAAAATGAGTGTAGATAAACAAA
<G  K  T  S  Y  N  E  K  F  I  K  S  V  D  I  Q  K
<_____ORF RF[4] C_____

       560        570        580        590        600
TTCTTTGGTGGAATTCTGAATGATAAAGACTATACTGCCATTTTTCTTAA
AAGAAACCACCTTAAGACTTACTATTTCTGATATGACGGTAAAAAGAATT
 <E  K  T  S  N  Q  I  I  F  V  I  S  G  N  K  K  F
<_____ORF RF[4] C_____

       610        620        630        640        650
AAAAGGCTAACTGAATTTCAGGATTTAATGATTCGAAAGCAGCCTCAATG
TTTTCCGATTGACTTAAAGTCCTAAATTACTAAGCTTTCGTCGGAGTTAC
                                                M>
                                                 ___>
  <F  A  L  Q  I  E  P  N  L  S  E  F  A  A  E  I
<_____ORF RF[4] C_____

       660        670        680        690        700
GCATTATCACACAAGATAGAAAGTATGGTAATGAAATCAAGCAACTCCAT
CGTAATAGTGTGTTCTATCTTTCATACCATTACTTTAGTTCGTTGAGGTA
 A  L  S  H  K  I  E  S  M  V  M  K  S  S  N  S  I>
_____ORF RF[3] _____>
<A  N  D  C  L  I  S  L  I  T  I  F  D  L  L  E  M
<_____ORF RF[4] C_____

       710        720        730        740        750
CTCAGGCAGTTGTATTTTACTTGAGACTTCTACATTGACAGCAATCTTTT
GAGTCCGTCAACATAAAATGAACTCTGAAGATGTAACTGTCGTTAGAAAA
  S  G  S  C  I  L  L  E  T  S  T  L  T  A  I  F>
_____ORF RF[3] _____>
<E  P  L  Q  I  K  S  S  V  E  V  N  V  A  I  K  K
<_____ORF RF[4] C_____

       760        770        780        790        800
TATTCTGAGCTTCTAAGATTTTTGCTGACAAGATACCCTTGACAGCATCG
ATAAGACTCGAAGATTCTAAAAACGACTGTTCTATGGGAACTGTCGTAGC
L  F>
_____>
 <N  Q  A  E  L  I  K  A  S  L  I  G  K  V  A  D
<_____ORF RF[4] C_____

       810        820        830        840        850
TTTTGAATATTAGCTAGATGGCCGATATTATAACGGGTATCCTGCAATTG
AAAACTTATAATCGATCTACCGGCTATAATATTGCCCATAGGACGTTAAC
<N  Q  I  N  A  L  H  G  I  N  Y  R  T  D  Q  L  Q
<_____ORF RF[4] C_____
```

Figure 9 (cont'd - 2)

```
        860        870        880        890        900
ATGTCCTGTTTTTTCTAAGATTTGATGGTAAATCTTTTCAATACTAGCTA
TACAGGACAAAAAAGATTCTAAACTACCATTTAGAAAAGTTATGATCGAT
 <H  G  T  K  E  L  I  Q  H  Y  I  K  E  I  S  A  L
<_____________________ORF RF[4] C_____________________

        910        920        930        940        950
AATCTTTATTTTCAATGCCTAATCTGAGGCTAGTTAAAATATTCAGATAA
TTAGAAATAAAAGTTACGGATTAGACTCCGATCAATTTTATAAGTCTATT
  <D  K  N  E  I  G  L  R  L  S  T  L  I  N  L  Y
<_____________________ORF RF[4] C_____________________

        960        970        980        990       1000
TCATGGCGGAAACTTCGAATATCCTTGTAAAGAGATTCTATTTGCTGACT
AGTACCGCCTTTGAAGCTTATAGGAACATTTCTCTAAGATAAACGACTGA
   M  A  E  T  S  N  I  L  V  K  R  F  Y  L  L  T>
 _____________________________________________________>
<D  H  R  F  S  R  I  D  K  Y  L  S  E  I  Q  Q  S
<_____________________ORF RF[4] C_____________________

       1010       1020       1030       1040       1050
ATACTGGGTGATATTTCGAATCTGAGCTTCCTTTTGTGCCATTATCTCAT
TATGACCCACTATAAAGCTTAGACTCGAAGGAAAACACGGTAATAGAGTA
 I  L  G  D  I  S  N  L  S  F  L  L  C  H  Y  L  I>
 _____________________________________________________>
 <Y  Q  T  I  N  R  I  Q  A  E  K  Q  A  M  I  E  N
<_____________________ORF RF[4] C_____________________

       1060       1070       1080       1090       1100
TTTGAACCTTTTGTTTGGTATATTGGCTTAAAAATGAGATCAGAATCAAA
AAACTTGGAAAACAAACCATATAACCGAATTTTTACTCTAGTCTTAGTTT
  L  N  L  L  F  G  I  L  A>
 ____________________________>
  <Q  V  K  Q  K  T  Y  Q  S  L  F  S  I  L  I  L
<_____________________ORF RF[4] C_____________________

       1110       1120       1130       1140       1150
AATAAAATAAGATAGACAATAACGACAAATTTACGAAATTTTAAAGTCGG
TTATTTTATTCTATCTGTTATTGCTGTTTAAATGCTTTAAAATTTCAGCC
<F  L  I  L  Y  V  I  V  V  F  K  R  F  K  L  T  P
<_____________________ORF RF[4] C_____________________

       1160       1170       1180       1190       1200
TATCACATTATAACTCTCTATAACATACAATACCTGTATTAAAAGGTAGT
ATAGTGTAATATTGAGAGATATTGTATGTTATGGACATAATTTTCCATCA
 <I  V  N  Y  S  E  I  V  Y  L  V  Q  I  L  L  Y  Y
<_____________________ORF RF[4] C_____________________

       1210       1220       1230       1240       1250
ATAGAAGCATAGTAATATTCATTGGAATCAAGCGTTTTTTGACCTTCATC
TATCTTCGTATCATTATAAGTAACCTTAGTTCGCAAAAAACTGGAAGTAG
  <L  L  M  T  I  N  M  P  I  L  R  K  K  V  K  M.
<_____________________ORF RF[4] C_____________________

       1260       1270       1280       1290       1300
TTGGTCAAACTATCTTTAAGTCGACCAATATCAACATTGAACACACTGAG
```

Figure 9 (cont'd - 3)

```
 AACCAGTTTGATAGAAATTCAGCTGGTTATAGTTGTAACTTGTGTGACTC
<K  T  L  S  D  K  L  R  G  I  D  V  N  F  V  S  L
<_____________________ORF RF[4] C_____________________

       1310       1320       1330       1340       1350
 AAAGAGGTAACTTAGCGCTATTCCTGCAAACTCGATCATATAGGTGGTTA
 TTTCTCCATTGAATCGCGATAAGGACGTTTGAGCTAGTATATCCACCAAT
 <F  L  Y  S  L  A  I  G  A  F  E  I  M  Y  T  T  I
<_____________________ORF RF[4] C_____________________

       1360       1370       1380       1390       1400
 TAATGCTACTGCCCATTACAATTCCTTGAGTTCCATCCAAGATAAAGAAT
 ATTACGATGACGGGTAATGTTAAGGAACTCAAGGTAGGTTCTATTTCTTA
  <I  S  S  G  M  V  I  G  Q  T  G  D  L  I  F  F
<_____________________ORF RF[4] C_____________________
                     <L  E  K  L  E  M  W  S  L  S  Y
                    <_____________________________________

       1410       1420       1430       1440       1450
 ATGATTGCCCGCCTAAACAAGTCAGAACTGGCAACAGGCAGCAGACCATA
 TACTAACGGGCGGATTTGTTCAGTCTTGACCGTTGTCCGTCGTCTGGTAT
<I  I  A  R  R  F  L  D  S  S  A  V  P  L  L  G  Y
<_____________________ORF RF[4] C_____________________
  <S  Q  G  G  L  C  T  L  V  P  L  L  C  C  V  M
<_____________________________________________

       1460       1470       1480       1490       1500
 AAATATATTTAGAGAAAGACTATTCTGTCTATTAAGATAAATTGATAAAG
 TTTATATAAATCTCTTTCTGATAAGACAGATAATTCTATTTAACTATTTC
 <F  I  N  L  S  L  S  N  Q  R  N  L  Y  I  S  L  A
<_____________________ORF RF[4] C_____________________

       1510       1520       1530       1540       1550
 CTATAAAATAAAGAGGCTCTGCAGGATAAAACAGGTTTACGTTCACCATC
 GATATTTTATTTCTCCGAGACGTCCTATTTTGTCCAAATGCAAGTGGTAG
  <I  F  Y  L  P  E  A  P  Y  F  L  N  V  N  V  M
<_____________________ORF RF[4] C_____________________

       1560       1570       1580       1590       1600
 GTAACAGCAATCATTATCAGAAAATTGCTTATCGAAAAAAGAGTTAATTC
 CATTGTCGTTAGTAATAGTCTTTTAACGAATAGCTTTTTTCTCAATTAAG
<T  V  A  I  M  I  L  F  N  S  I  S  F  L  T  L  E
<_____________________ORF RF[4] C_____________________

       1610       1620       1630       1640       1650
 CTTTTTCGATAAAGTGACATTACTTACCTTAGAAAATAGAAACAAGAGAA
 GAAAAAGCTATTTCACTGTAATGAATGGAATCTTTTATCTTTGTTCTCTT
 <K  K  S  L  T  V  N  S  V  K  S  F  L  F  L  L  F
<_____________________ORF RF[4] C_____________________

       1660       1670       1680       1690       1700
 ATAGAACGGTTAGATAAGTTAATAAACCATTTGAAAGTATCATTAAGGCT
 TATCTTGCCAATCTATTCAATTATTTGGTAAACTTTCATAGTAATTCCGA
  <L  V  T  L  Y  T  L  L  G  N  S  L  I  M  L  A
<_____________________ORF RF[4] C_____________________

       1710       1720       1730       1740       1750
```

Figure 9 (cont'd - 4)

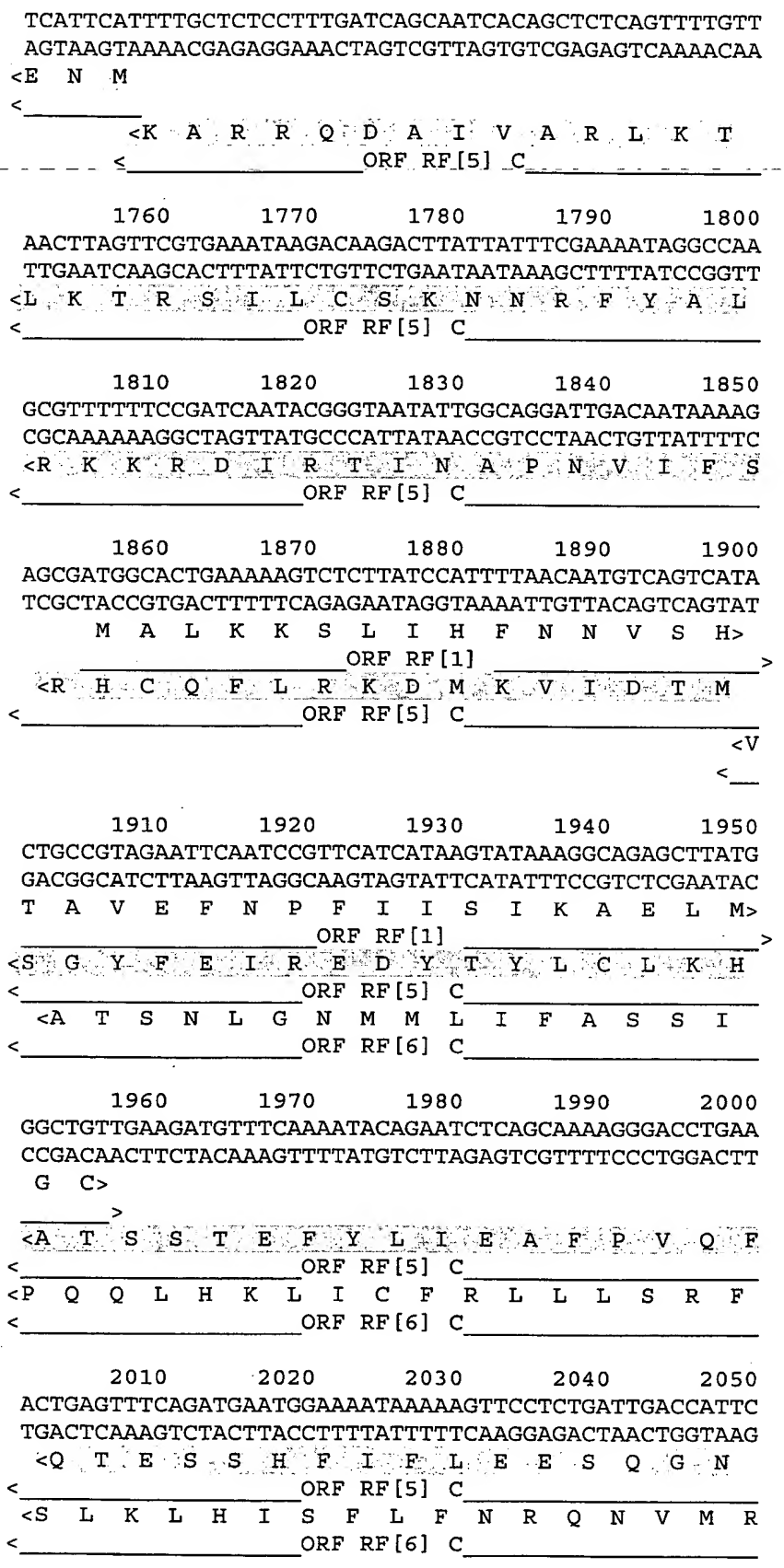

Figure 9 (cont'd - 5)

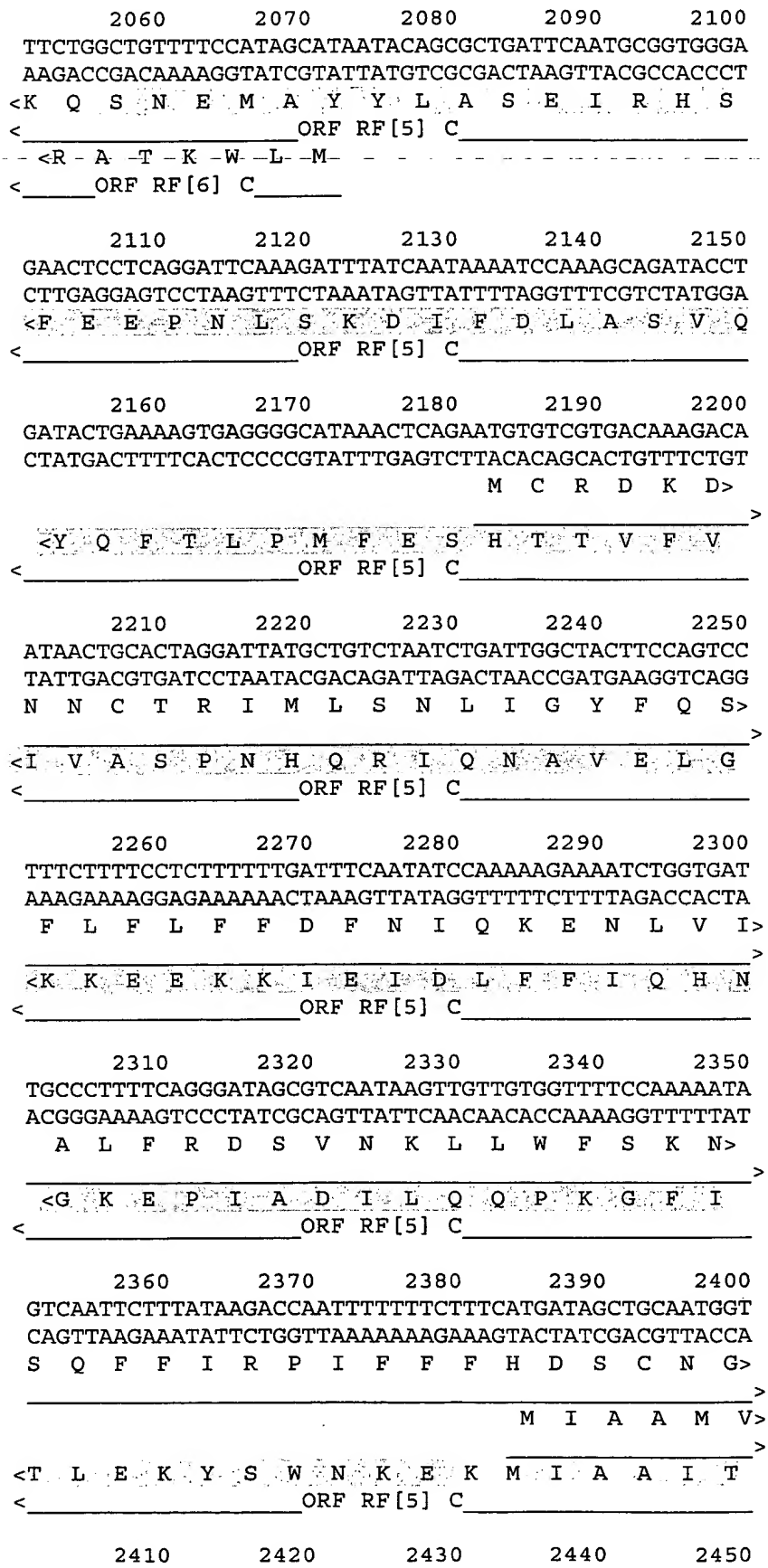

Figure 9 (cont'd - 6)

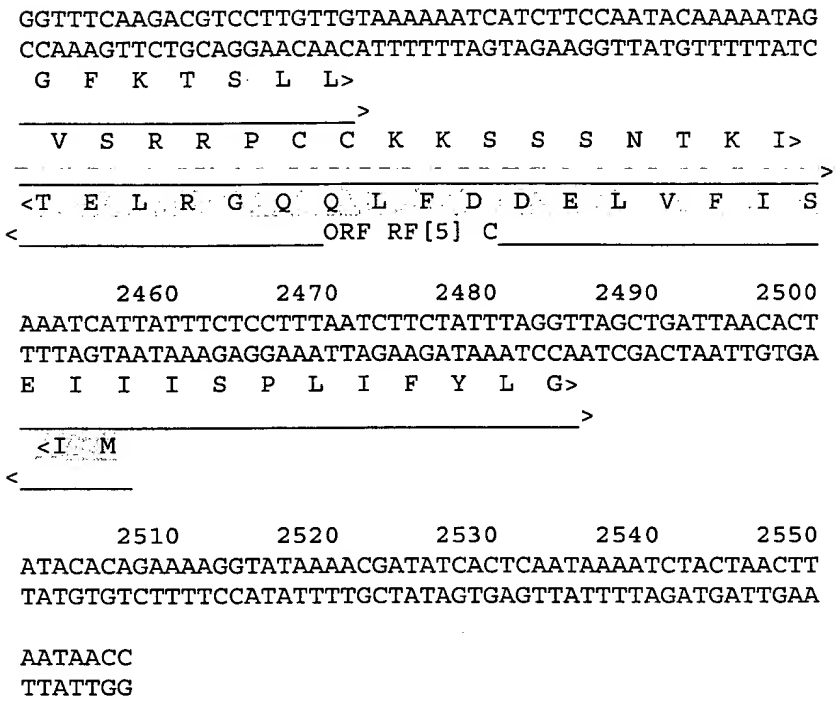

Figure 10

A.

ATGGAAGAAGATTTTGAAATTGTTTTTAATAAGGTTAAGCCAATTGTATGGAAATTAAG
CCGTTATTACTTTATTAAAATGTGGACTCGTGAAGATTGGCAACAAGAGGGAATGTTGA
TTTTGCACCAATTATTAAGGGAACATCCAGAATTAGAAGAGGATGATACAAAATTGTAT
ATCTATTTTAAGACACGTTTTTCTAATTACATTAAAGATGTTTTGCGTCAGCAAGAAAG
TCAGAAACGTCGTTTTAATAGAATGTCTTATGAAGAAGTCGGTGAGATTGAACACTGTT
TGTCAAGTGGCGGTATGCAATTGGATGAATATATTTTATTTCGTGATAGTTTGCTTGCA
TATAAACAAGGTCTGAGTACTGAAAAGCAAGAGCTGTTTGAGCGCTTGGTAGCAGGAGA
GCACTTTTTGGGAAGGCAAAGTATGCTGAAAGATTTACGTAAAAAATTAAGTGATTTTA
AGGAAAAA

B.

MEEDFEIVFNKVKPIVWKLSRYYFIKMWTREDWQQEGMLILHQLLREHPELEEDDTKLY
IYFKTRFSNYIKDVLRQQESQKRRFNRMSYEEVGEIEHCLSSGGMQLDEYILFRDSLLA
YKQGLSTEKQELFERLVAGEHFLGRQSMLKDLRKKLSDFKEK

C.

GTAAATAAAACAGCCAGTTAAGATGGGACATTTATGTCCTGTTCTTAAAGTCTTTTTCG
TTTTATAATAATTTTATTATAAAAGGAGGTCATCGTAATAGATGGAAGAAGATTTTGAA
ATTGTTTTTAATAAGGTTAAGCCAATTGTATGGAAATTAAGCCGTTATTACTTTATTAA
AATGTGGACTCGTGAAGATTGGCAACAAGAGGGAATGTTGATTTTGCACCAATTATTAA
GGGAACATCCAGAATTAGAAGAGGATGATACAAAATTGTATATCTATTTTAAGACACGT
TTTTCTAATTACATTAAAGATGTTTTGCGTCAGCAAGAAAGTCAGAAACGTCGTTTTAA
TAGAATGTCTTATGAAGAAGTCGGTGAGATTGAACACTGTTTGTCAAGTGGCGGTATGC
AATTGGATGAATATATTTTATTTCGTGATAGTTTGCTTGCATATAAACAAGGTCTGAGT
ACTGAAAAGCAAGAGCTGTTTGAGCGCTTGGTAGCAGGAGAGCACTTTTTGGGAAGGCA
AAGTATGCTGAAAGATTTACGTAAAAAATTAAGTGATTTTAAGGAAAAATAGTTAAAAA
GGGAAAGAATGGAACATGTGATTGTACCATTCTTTTTGGTTGAAAATTAAGAAAAGTTA
TTATAAATTATTGGTTTAACATGCCATATTA

Figure 11

A.

ATGAAACAAGTTATTTATGTTGTTTTAATCGTCATAGCCGTTAACATTCTCTTAGAGAT
TATCAAAAGAGTAACAAAAAGGGGAGGGACAGTTTCGTCATCTAATCCTTTACCAGATG
GGCAGTCTAAGTTGTTTTGGCGCAGACATTATAAGCTAGTACCTCAGATTGATACCAGA
GACTGTGGGCCGGCAGTGCTGGCATCTGTTGCAAAGCATTACGGATCTAATTACTCTAT
CGCTTATCTGCGGGAACTCTCAAAGACTAACAAGCAGGGAACAACAGCTCTTGGCATTG
TTGAAGCTGCTAAAAAGTTAGGCTTTGAAACACGCTCTATCAAGGCGGATATGACGCTT
TTTGATTATAATGATTTGACCTATCCTTTTATCGTCCATGTGATTAAAGGAAAACGTCT
GCAGCATTATTATGTCGTCTATGGCAGCCAGAATAATCAGCTGATTATTGGAGATCCTG
ATCCTTCAGTTAAGGTGACTAGGATGAGTAAGGAACGCTTTCAATCAGAGTGGACAGGC
CTTGCAATTTTCCTAGCTCCTCAGCCTAACTATAAGCCTCATAAAGGTGAAAAAAATGG
TTTGTCTAATTTCTTCCCGTTGATCTTTAAGCAGAAAGCTTTGATGACTTATATTATCA
TAGCTAGCTTGATTGTGACGCTCATTGATATTGTCGGATCATACTATCTCCAAGGAATA
TTGGACGAGTACATTCCTGATCAGCTGATTTCAACTTTAGGAATGATTACGATTGGTCT
GATAATAACCTATATTATCCAGCAGGTCATGGCTTTTGCAAAAGAATACCTCTTGGCCG
TACTCAGTTTGCGTTTAGTCATTGATGTTATCCTGTCTTATATCAAACATATTTTTACG
CTTCCTATGTCTTTCTTTGCGACAAGGCGAACAGGAGAAATCACGTCTCGTTTTACAGA
TGCCAATCAGATTATTGATGCTGTAGCGTCAACCATCTTTTCAATCTTTTTAGATATGA
CTATGGTAATTTTGGTTGGTGGGGTTTTGTTGGCGCAAAACAATAACCTTTTCTTTCTA
ACCTTGCTCTCCATTCCGATTTATGCCATCATTATTTTTGCTTTCTTGAAACCCTTTGA
GAAAATGAATCACGAAGTGATGGAAAGCAATGCTGTGGTAAGTTCTTCTATCATTGAAG
ATATCAATGGGATGGAAACCATTAAATCACTCACAAGTGAGTCCGCTCGTTATCAAAAC
ATTGATAGTGAATTTGTTGATTATTTGGAGAAAAACTTTAAGCTACACAAGTATAGTGC
CATTCAAACCGCATTAAAAAGCGGTGCTAAGCTTATCCTCAATGTTGTCATTCTCTGGT
ATGGCTCTCGTCTAGTTATGGATAATAAAATCTCAGTTGGTCAGCTTATCACCTTTAAT
GCTTTGCTGTCTTATTTCTCAAATCCAATTGAAAATATTATCAATCTGCAATCCAAACT
GCAGTCAGCTCGCGTTGCCAATACACGTCTTAATGAGGTCTATCTTGTCGAATCTGAAT
TTGAAAAAGACGGCGATTTATCAGAAAATAGCTTTTTAGATGGTGATATTTCGTTTGAA
AATCTTTCTTATAAATATGGATTTGGGCGAGATACCTTATCAGATATTAATTTATCAAT
CAAAAAAGGCTCCAAGGTCAGTCTAGTTGGAGCCAGTGGTTCTGGTAAAACAACTTTGG
CTAAACTGATTGTCAATTTCTACGAGCCTAACAAGGGGATTGTTCGAATCAATGGCAAT
GATTTAAAAGTTATTGATAAGACAGCTTTGCGGCGGCATATTAGCTATTTGCCGCAACA
GGCCTATGTTTTTAGTGGCTCTATTATGGATAATCTCGTTTTAGGAGCTAAAGAAGGAA
CGAGTCAGGAAGACATTATTCGTGCTTGTGAAATTGCTGAAATCCGCTCGGACATTGAA
CAAATGCCTCAGGGCTATCAGACAGAGTTATCAGATGGTGCCGGTATTTCTGGCGGTCA
AAAACAGCGGATTGCTTTAGCTAGGGCCTTATTAACACAGGCACCGGTTTTGATTCTGG
ATGAAGCCACCAGCAGTCTTGATATTTTGACAGAAAAGAAAATTATCAGCAATCTCTTA
CAGATGACGGAGAAAACAATAATTTTTGTTGCCCACCGCTTAAGCATTTCACAGCGTAC
TGACGAAGTCATTGTCATGGATCAGGGAAAAATTGTTGAACAAGGCACTCATAAGGAAC
TTTTAGCTAAGCAAGGTTTCTATTATAACCTGTTTAAT

Figure 11 (cont'd)

B.

MKQVIYVVLIVIAVNILLEIIKRVTKRGGTVSSSNPLPDGQSKLFWRRHYKLVPQIDTR
DCGPAVLASVAKHYGSNYSIAYLRELSKTNKQGTTALGIVEAAKKLGFETRSIKADMTL
FDYNDLTYPFIVHVIKGKRLQHYYVVYGSQNNQLIIGDPDPSVKVTRMSKERFQSEWTG
LAIFLAPQPNYKPHKGEKNGLSNFFPLIFKQKALMTYIIIASLIVTLIDIVGSYYLQGI
LDEYIPDQLISTLGMITIGLIITYIIQQVMAFAKEYLLAVLSLRLVIDVILSYIKHIFT
LPMSFFATRRTGEITSRFTDANQIIDAVASTIFSIFLDMTMVILVGGVLLAQNNNLFFL
TLLSIPIYAIIIFAFLKPFEKMNHEVMESNAVVSSSIIEDINGMETIKSLTSESARYQN
IDSEFVDYLEKNFKLHKYSAIQTALKSGAKLILNVVILWYGSRLVMDNKISVGQLITFN
ALLSYFSNPIENIINLQSKLQSARVANTRLNEVYLVESEFEKDGDLSENSFLDGDISFE
NLSYKYGFGRDTLSDINLSIKKGSKVSLVGASGSGKTTLAKLIVNFYEPNKGIVRINGN
DLKVIDKTALRRHISYLPQQAYVFSGSIMDNLVLGAKEGTSQEDIIRACEIAEIRSDIE
QMPQGYQTELSDGAGISGGQKQRIALARALLTQAPVLILDEATSSLDILTEKKIISNLL
QMTEKTIIFVAHRLSISQRTDEVIVMDQGKIVEQGTHKELLAKQGFYYNLFN

C.

ATGGATCCTAAATTTTTACAAAGTGCAGAATTTTATAGGAGACGCTATCATAATTTTGC
GACACTATTAATTGTTCCTTTGGTCTGCTTGATTATCTTCTTGGTCATATTCCTTTGTT
TTGCTAAAAAAGAAATTACAGTGATTTCTACTGGTGAAGTTGCACCAACAAAGGTTGTA
GATGTTATCCAATCTTACAGTGACAGTTCAATCATTAAAAATAATTTAGATAATAATGC
AGCTGTTGAGAAGGGAGACGTTTTAATTGAATATTCAGAAAATGCCAGTCCAAACCGTC
AGACTGAACAAAAGAATATTATAAAAGAAAGACAAAAACGAGAAGAGAAGGAAAAGAAA
AAACACCAAAAGAGCAAGAAAAAGAAGAAGTCTAAGAGCAAGAAAGCTTCCAAAGATAA
GAAAAAGAAATCGAAAGACAAGGAAAGCAGCTCTGACGATGAAAATGAGACAAAAAAGG
TTTCGATTTTTGCTTCAGAAGATGGTATTATTCATACCAATCCCAAATATGATGGTGCC
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AAAAGTGTTAATCACCTATTATGCTTCTTCTGATGATGTTGTTTCTATGAAAAAGGGGC
AAACCGCTCGTCTTTCCTTGGAAAAAAAGGGAAATGACAAGGTTGTTATTGAAGGAAAA
ATTAACAATGTCGCTTCATCAGCAACTACTACTAAAAAAGGAAATCTCTTTAAGGTTAC
TGCCAAAGTAAAGGTTTCTAAGAAAAATAGCAAACTCATCAAGTATGGTATGACAGGCA
AGACAGTCACTGTCATTGATAAAAAGACTTATTTTGATTATTTCAAAGATAAATTACTG
CATAAAATGGATAAT

D.

MDPKFLQSAEFYRRRYHNFATLLIVPLVCLIIFLVIFLCFAKKEITVISTGEVAPTKVV
DVIQSYSDSSIIKNNLDNNAAVEKGDVLIEYSENASPNRQTEQKNIIKERQKREEKEKK
KHQKSKKKKKSKSKKASKDKKKKSKDKESSSDDENETKKVSIFASEDGIIHTNPKYDGA
NIIPKQTEIAQIYPDIQKTRKVLITYYASSDDVVSMKKGQTARLSLEKKGNDKVVIEGK
INNVASSATTTKKGNLFKVTAKVKVSKKNSKLIKYGMTGKTVTVIDKKTYFDYFKDKLL
HKMDN

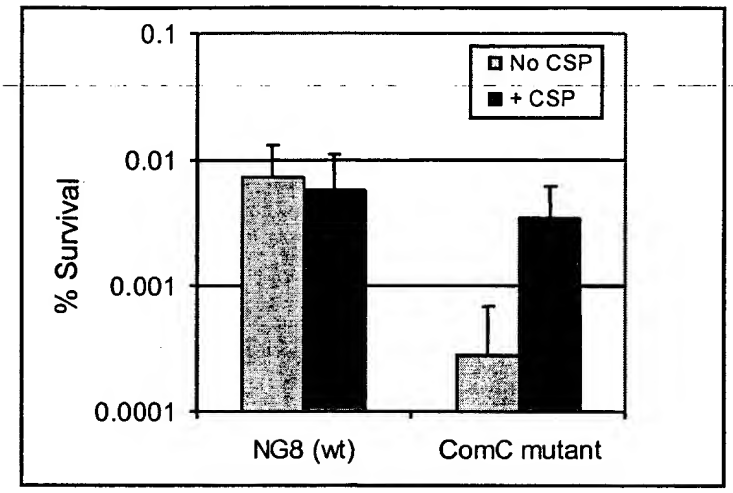

Figure 12